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Diagnostic Problems in a Case With Mucometrocolpos, Polydactyly, Congenital Heart Disease, and Skeletal Dysplasia

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Mucometrocolpos is the distention of the uterus and vagina caused by obstruction to the drainage of genital secretions. Although most cases of mucometrocolpos are sporadic, it may be part of an autosomal recessive condition, known as McKusick-Kaufman syndrome (MKS), including postaxial polydactyly and congenital heart disease as main findings. The diagnosis may be difficult when the presence of additional findings creates an overlap with other syndromes. We report on a female infant with mucometrocolpos, postaxial polydactyly, congenital heart disease, short limbs, short ribs, and chest constriction. The clinicopathological findings are described and discussed in the context of the phenotypic spectrums of MKS and mucometrocolpos concomitant with Ellis van Creveld syndrome. © 1996 Wiley-Liss, Inc.

KEY WORDS: mucometrocolpos (hydrometrocolpos), McKusick Kaufman syndrome, Ellis van Creveld syndrome (chondroectodermal dysplasia), oral-facial-skeletal syndromes

INTRODUCTION

Among the urogenital anomalies, mucometrocolpos—the distention of the uterus and vagina caused by obstruction to the drainage of genital secretions—is relatively rare with an estimated birth prevalence of < 1 in 16,000 females [Westerhout et al., 1964]. Although most cases are sporadic, mucometrocolpos may be associated with the autosomal recessive McKusick-Kaufman syndrome (MKS), also characterized by postaxial polydactyly and congenital heart disease [McKusick et al., 1964, Robinow and Shaw, 1979]. A great phenotypic variability occurs in this syndrome, making its diagnosis and nosology quite challenging.

We report on a case of MKS that illustrates the prenatal and postnatal diagnostic problems and stresses the importance of a correct and timely diagnosis.

CLINICAL REPORT

A 29-year-old woman, gravida 3, para 2, was referred at 35 weeks gestation to the High Risk Pregnancy Unit for further management of a fetal abdominal mass and short limbs that were detected sonographically. Her familial and past medical histories were uneventful. Her previous gestations had ended in the delivery of two healthy infants, a girl and a boy. The course of the pregnancy appeared normal until the sonographic detection of the following findings: severe abdominal distention with chest restriction, a retrovesical centropelvic rounded mass with midlevel echoes, measuring 8 cm in diameter (Fig. 1), short limbs with a femur length of 46 mm (compatible with a gestational age of 26 weeks), humerus length of 38 mm (compatible with a gestational age of 26 weeks), and tibia length of 47 mm (compatible with a gestational age of 29 weeks). Polydactyly was detected in both hands. Amniotic fluid was normal. A presumptive diagnosis of hemorrhagic ovarian cyst with skeletal dysplasia was made.

The patient underwent spontaneous labor at 36 weeks and delivered a female infant weighing 3,500 g (95th centile) and measuring 45 cm (5th centile). The newborn infant died within 1 hour after an unsuccessful attempt at resuscitation.

Examination of the infant showed abdominal distention reaching up to the umbilicus. Thoracic restriction was apparent. The limbs were short with extreme shortness of the distal phalanxes. Nail hypoplasia was noted. The anorectal region seemed superficially normal, but no vaginal opening could be found. The urethra was normally placed and easily catheterized.

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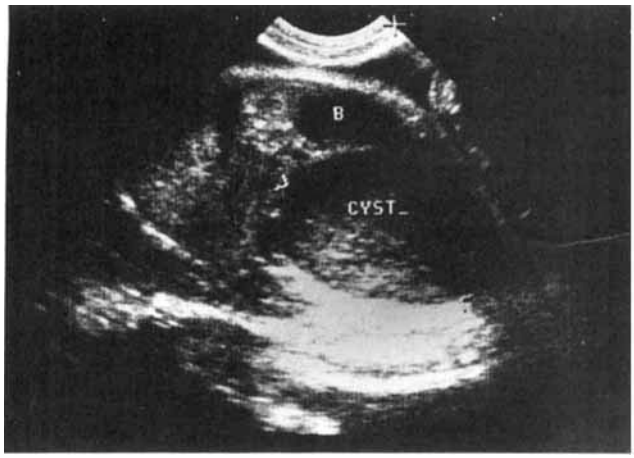

Fig. 1. Longitudinal scan of the lower fetal abdomen showing a retrovesical centrally located cystic mass (C) having midlevel echoes. B, urinary bladder.

On X-rays, the limbs were short, chest restriction was evident, iliac bones were small with flattened acetabular roofs. Premature ossification of the femoral epiphyses was noted (Fig. 2). Postaxial polydactyly of both hands was concomitant with syndactyly of the fourth and fifth digits and clinodactyly of the fifth finger of the left hand. Moreover, there was fusion of third and fourth metacarpals on the right. Distal phalanges were not ossified bilaterally (Fig. 3).

Fig. 2. Skeletal roentgen showing short ribs, chest constriction, short limbs, small iliac bones with flattened acetabular roofs, premature ossification of the femoral epiphyses and normal vertebral bodies.

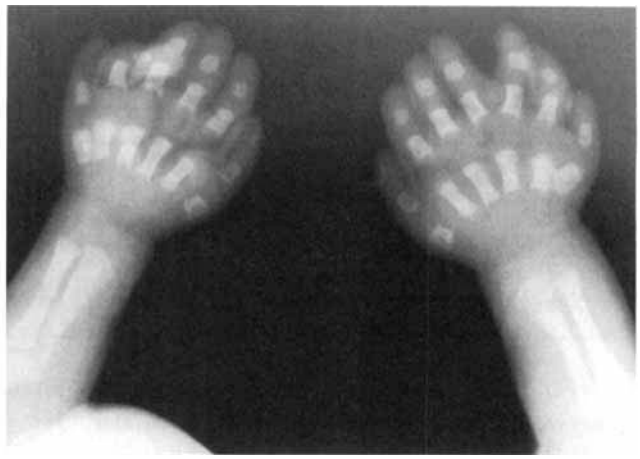

Fig. 3. Roentgen showing postaxial polydactyly of both hands (7 phalanxes on the right and 6 on the left) concomitant with syndactyly of the right hand and clinodactyly of the fifth finger of the left hand. The 5th and 6th right metacarpal bones are fused. Distal phalanxes are not ossified.

Necropsy showed that the cystic mass reaching up to the umbilicus was due to distal vaginal atresia (Type III), according to Spencer [Spencer and Levy, 1962]. The slimy cloudy secretions of > 200 cc were produced by uterine and cervical mucosae that distended the uterus and the vagina, thus creating the mucometrocolpos (Fig. 4 a,b). A ventricular septal defect was also detected. Clinical, radiological, and pathological findings of skeletal dysplasia seemed to be compatible with Ellis van Creveld (EVC) syndrome.

DISCUSSION

The rarity of mucometrocolpos can create difficulties both in its prenatal and postnatal diagnosis. The presumptive diagnosis of a cystic mass with midlevel echoes posterior to the bladder and anterior to the spine include the following: abdominal cyst, ovarian cyst, urachal cyst, mesenteric cyst, gastrointestinal duplication cyst, distended rectum, sacral teratoma, and mucometrocolpos. In one reported case, a cystic mass identified as a mucometrocolpos could be seen protruding into the vagina [Davis et al., 1984]. Unless this finding is present, a precise diagnosis is reported not to be possible by sonography. However, the finding of a perineal involvement is considered to be quite specific, and several authors have reported the antenatal diagnosis of mucometrocolpos [Davis et al., 1984; Hill and Hirsch, 1985, Boulot et al., 1991]. In the present case, necropsy only allowed the diagnosis of mucometrocolpos.

The issues of phenotypic overlap and heterogeneity between similar syndromes sharing various combinations of skeletal and genital anomalies are a matter of debate. Mucometrocolpos, postaxial polydactyly, and congenital heart disease are the cardinal findings of the MKS in affected females. If identical mutation(s) are

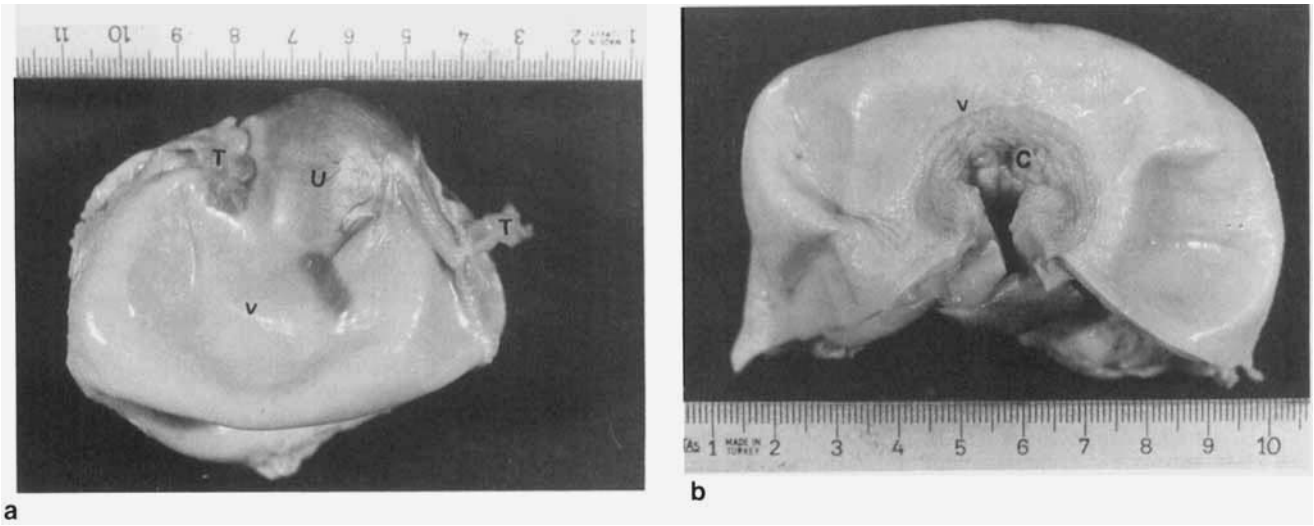

Fig. 4. **a,b**: Gross macroscopic appearance of mucometrocolpos, showing distention of the uterus (U) and vagina (v). Cervix (C), Fallopian tube (T).

responsible for all cases of this condition, the same spectrum of abnormalities should be expected both in familial and sporadic cases. Therefore, if sufficient familial cases are available, the observed clinical variability might be used to determine whether or not a sporadic case really represents the syndrome. The MKS, in which the numbers of familial and sporadic cases are nearly equal, may be a suitable model to carry out such a comparison [Lurie and Wulfsberg, 1994].

Sporadic cases of the MKS can be subdivided into three groups [Lurie and Wulfsberg, 1994]: (1) Patients who have main clinical findings including mucometrocolpos, postaxial polydacytyly, congenital heart disease, anal atresia/stenosis, Hirschsprung disease, cystic kidneys, syndactyly, retinitis pigmentosa, umbilical hernia, short perineum, hydronephrosis/hydrourether (secondary), hypospadias, and cryptorchidism. (2) Patients who have the main clinical findings with one additional finding, which may be intestinal malrotation [Notter and Chabal, 1959], hip dislocation [Campbell and Zaidi, 1962], oligodactyly [Westerhout et al., 1964], hemihypertrophy [Pare and Elhilali, 1972], albinism [Wilson et al., 1978], microcephaly [Robinow and Shaw, 1979], cleft palate [Nguyen et al., 1984], brachydactyly [Farrell et al., 1986], tracheal stenosis [Brouard et al., 1988], eye staphyloma [Cantani et al., 1991], nonimmune hydrops [Rosen and Bocian, 1991], complete tracheal ring [Cuyler and Giovanetti, 1992], esophageal atresia with tracheoesophageal fistula [Pul et al., 1994], polythelia [Lurie and Wulfsberg, 1994], hypoplastic kidney [Franke et al., 1988], or optic nerve atrophy [Richards et al., 1980], (3) patients with two or more findings, not mentioned in familial cases. In these patients, the diagnosis may be difficult or doubtful, because of the issues of phenotypic overlap and heterogeneity between similar syndromes sharing various combinations of anomalies.

We consider the present case as belonging to the third category according Lurie and Wulfsberg [1994]. The mucometrocolpos, postaxial polydactyly, and congenital heart disease are the constant manifestations of MKS. However, EVC syndrome, in the category of short rib polydactyly (SRP) syndromes also may be associated with congenital heart disease and urogenital anomalies, suggesting the possible diagnosis of mucometrocolpos concomitant with EVC syndrome, as first reported by Akoun and Bagard [1956]. At least three other reports describing the association between short limb dwarfism, short ribs, lung hypoplasia, hydrometrocolpos and postaxial polydactyly have been available in the literature [Chitayat et al., 1987; Yang et al., 1987; Meinecke and Hayek, 1990]; however, these cases also may be regarded as the examples of a new syndrome or unusual (with hydrometrocolpos) cases of the Mohr-Majewski or the Jeune syndrome, or falling within the spectrum of MKS. Nevertheless, the best approach for these transient cases, including the present case, may be to consider them in the spectrum of Oral-Facial-Skeletal (OFS) syndromes, proposed by Neri et al. [1995].

In a review of transitional patients falling within a community of conditions, Neri et al. [1995] proposed the subsumption of oral-facial-digital syndromes (OFD), SRP, Pallister Hall, Hydrolethalus, and McKusick Kaufman syndromes under the common heading of OFS syndromes as the degree of clinical overlap of the other syndromes is so impressive, and each condition shares virtually all of its characteristic traits with all other conditions. It seems possible that lumping together as OFS syndrome is not only justified on clinical, but also nosologic grounds. The bulk of OFS has autosomal recessive (AR) transmission. In theory, the AR subtypes could all be related causally to a single focus with several mutant alleles, giving rise to a variety of different homozygotes and compound heterozygotes. It is equally possible and even more likely that locus heterogeneity extends into the AR syndromes, thus providing a limited number of loci, each with a number of alleles sufficient to generate the nearly 20 distinct clinical entities belonging to the OFS syndrome family. The

least likely explanation is that each of these corresponds to a distinct locus due to the presence of the transitional cases [Neri et al., 1995]. Recently, Francomano et al. [1995] reported the linkage for the EVC syndrome gene to markers on the distal short arm of human chromosome 4p16 that will probably provide the possibility to improve our understanding of the nosology of these disorders in the future.

Although the nosology is still uncertain, prenatal diagnosis of mucometrocolpos could make it possible to drain the accumulating secretions under ultrasonic guidance either in the prenatal or in the immediate postnatal period, thereby limiting the abdominal distention and the respiratory distress. Moreover, successful abdominoperineal pull through operations for the Type III distal vaginal atresia have also been reported as the definitive treatment of mucometrocolpos in the postnatal period [Ramenofsky and Raffensberger, 1971].

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